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Amendment and Response

Serial No.: 10/694,385

Confirmation No.: 5758

Filed: 27 October 2003

For: METHODS FOR CREATING A COMPOUND LIBRARY AND IDENTIFYING LEAD CHEMICAL
TEMPLATES AND LIGANDS FOR TARGET MOLECULES

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1-17. (Canceled)

18. (Currently amended) A method of identifying a compound that binds to a target molecule, the method comprising:

selecting a library comprising test compounds, wherein each test compound is selected based on having ~~has~~ a solubility in deuterated water of at least about 1 mM at room temperature[~~[,]~~] and ~~has~~ a molecular weight of no greater than about 350 grams/mole;

providing a plurality of mixtures of the test compounds, each mixture being in a sample reservoir;

introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

providing a nuclear magnetic resonance spectrometer equipped with a flow-injection probe;

transferring each test sample from the sample reservoir into the flow-injection probe;

collecting a relaxation-edited nuclear magnetic resonance spectrum on each test sample in each sample reservoir; and

comparing the spectra of each test sample to the spectra taken under the same conditions in the absence of the target molecule to identify test compounds that bind to the target molecule;

wherein the concentration of target molecule and each test compound in each sample reservoir is no greater than about 100 μ M; and

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wherein the ratio of target molecule to each test compound in each sample
reservoir is about 1:1.

19. (Original) The method of claim 18 wherein each mixture is in a sample reservoir of a multiwell sample holder.
20. (Original) The method of claim 19 wherein the multiwell sample holder is a 96-well microtiter plate.
21. (Canceled)
22. (Canceled)
23. (Original) The method of claim 18 wherein collecting a relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited nuclear magnetic resonance spectrum.
24. (Original) The method of claim 23 wherein collecting a 1D relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited ¹H nuclear magnetic resonance spectrum.
25. (Previously Presented) The method of claim 18 wherein the mixture of test compounds comprises at least about 3 compounds, each having at least one distinguishable resonance in a 1D NMR spectrum of the mixture.
26. (Previously Presented) The method of claim 25 wherein the mixture of test compounds comprises at least about 6 compounds.

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27. (Canceled)

28. (Previously Presented) The method of claim 18 wherein the concentration of target molecule and each test compound in each sample reservoir is no greater than about 50 μ M.

29. (Previously Presented) The method of claim 18 further wherein comparing spectra to identify test compounds that bind to the target molecule comprises identifying a test compound that binds to the target molecule with a dissociation constant at least about 100 μ M.

30. (Original) The method of claim 18 wherein the target molecule is a protein.

31-45. (Canceled)

46. (New) The method of claim 18 wherein the library comprises at least 75 and no more than about 10,000 test compounds.

47. (New) The method of claim 46 wherein the library comprises at least 300 compounds.

48. (New) The method of claim 46 wherein the library comprises at least 2000 compounds.

49. (New) A method of identifying a compound that binds to a target molecule, the method comprising:

selecting a library comprising at least 75 and no more than about 10,000 test compounds, wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature, and has a molecular weight of no greater than about 350 grams/mole;

providing a plurality of mixtures of the test compounds, each mixture being in a sample reservoir;

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introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

providing a nuclear magnetic resonance spectrometer equipped with a flow-injection probe;

transferring each test sample from the sample reservoir into the flow-injection probe;

collecting a relaxation-edited nuclear magnetic resonance spectrum on each test sample in each sample reservoir; and

comparing the spectra of each test sample to the spectra taken under the same conditions in the absence of the target molecule to identify test compounds that bind to the target molecule;

wherein the concentration of target molecule and each test compound in each sample reservoir is no greater than about 100 μ M; and

wherein the ratio of target molecule to each test compound in each sample reservoir is about 1:1.

50. (New) The method of claim 49 wherein the library comprises at least 300 compounds.
51. (New) The method of claim 49 wherein the library comprises at least 2000 compounds.